MELBOURNE HEALTH

The role clinical trials pharmacists in study medication adherence

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Melbourne Health
Australia


Norwegian Sea
Sweden
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Russia
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Turkmenistan
Sea of Japan
China
South Korea
Japan
Tunisia
Morocco
Syria
Iraq
Iran
Afghanistan
Pakistan
East China Sea
Algeria
Libya
Egypt
Western Sahara
Saudi Arabia
Nepal
India
Myanmar (Burma)
Oman
Mauritania
Mali
Niger
Chad
Sudan
Yemen
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Bay of Bengal
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Philippines
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Guinea
Nigeria
Ghana
Gulf of Aden
Arabian Sea
Gulf of Thailand
South Sudan
Ethiopia
Laccadive Sea
Gulf of Guinea
Somalia
Malaysia
Kenya
Gabon
Indonesia
DR Congo
Banda Sea
Papua New Guinea
Tanzania
Arafura Sea
Angola
Zambia
Mozambique
Coral Sea
Namibia
Zimbabwe
Madagascar
Botswana
Indian Ocean
NT
QLD
Australia
WA
SA
South Africa
Great Australian Bight

Melbourne Health

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- Opened 20 March 1846
- Colony of Victoria in 1851
- The University of Melbourne in 1854
- State of Victoria in 1901

Melbourne Health

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The Royal
Melbourne Hospital
Victorian Comprehensive Cancer Centre


ROYAL MELBOURNE HOSPITAL
The Royal Melbourne Hospital

Melbourne Health

MELBOURNE HEALTH

First in Care, Research and Learning

CARING
EXCELLENCE
INTEGRITY
RESPECT
UNITY

- A major health care provider in Victoria, Australia
- Almost 100,000 inpatient services in one year
- More than 645,000 outpatient appointments/year
- More than 8,000 staff employed
- About 1,400 beds

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Overview

- Treatment Compliance / Medication adherence
- Medication adherence in clinical trials
- Roles of clinical trials pharmacist in improving medication adherence
- Other roles of clinical trials pharmacist

Compliance and Adherence

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- Compliance
  - Patient's behaviours coincide with healthcare providers' recommendations for health and medical advice in terms of taking medications, following diets or executing life style changes
- Adherence
  - The degree of extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage and frequency

Other terms

- Persistence
  - The length of time between initiation and discontinuation of therapy
  - Medication adherence encompasses the process of initiation of appropriate dosing and persistence
  - Over-persistence
  - Under-persistence
- Over-usage
- Under-usage

By MARY BROPHY MARCUS / CBS NEWS / July 18, 2016, 4:53 PM

Many seniors are taking their medicines in risky ways



A new study of older adults shows more than half take five or more medicines a day, yet few take their medications the right way. JORGE SALCEDO, GETTY IMAGES/ISTOCKPHOTO

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A new study of older adults shows more than half take five or more medicines a day, yet few take their medications the right way. Not using enough medicine was found to be a serious problem -- with major repercussions for their health.

Belgian researchers from Ghent University in Belgium studied 503 adults over the age of 80 for a year and a half. The participants were described as cognitively fit (not suffering from dementia) and living in the community, not hospitalized or in a nursing home.

Medication underuse -- not taking enough of prescribed drugs -- turned out to be a big problem, according to the study published in the British Journal of Clinical Pharmacology. Two-thirds of the patients did not take the full amount of the medications they needed. Misuse -- for example, taking a drug longer than recommended, or at the wrong time of day -- happened in 56 percent of cases. Forty percent both misused and underused various medications.

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Treatment Compliance

- Purpose of treatment
  - To achieve certain desired outcomes in the patients concerned
  - Not achievable if the patient is not compliant
  - Taking medications as prescribed
  - Following advice on diet, exercise or activity
- Poor Compliance – failure to follow doctor's advice ➔ Treatment Failure



"LET'S SEE... WE'VE TAKEN YOU OFF SMOKING, DRINKING AND RICH FOOD. WHAT ELSE DO YOU ENJOY?"

Medication Adherence

- The extent to which patients take medications as prescribed by their healthcare providers
  - Taking the prescribed medications at the correct times and in the right amounts
- Monitoring medication adherence
  - Optimal adherence
  - Variable adherence

Medication Adherence

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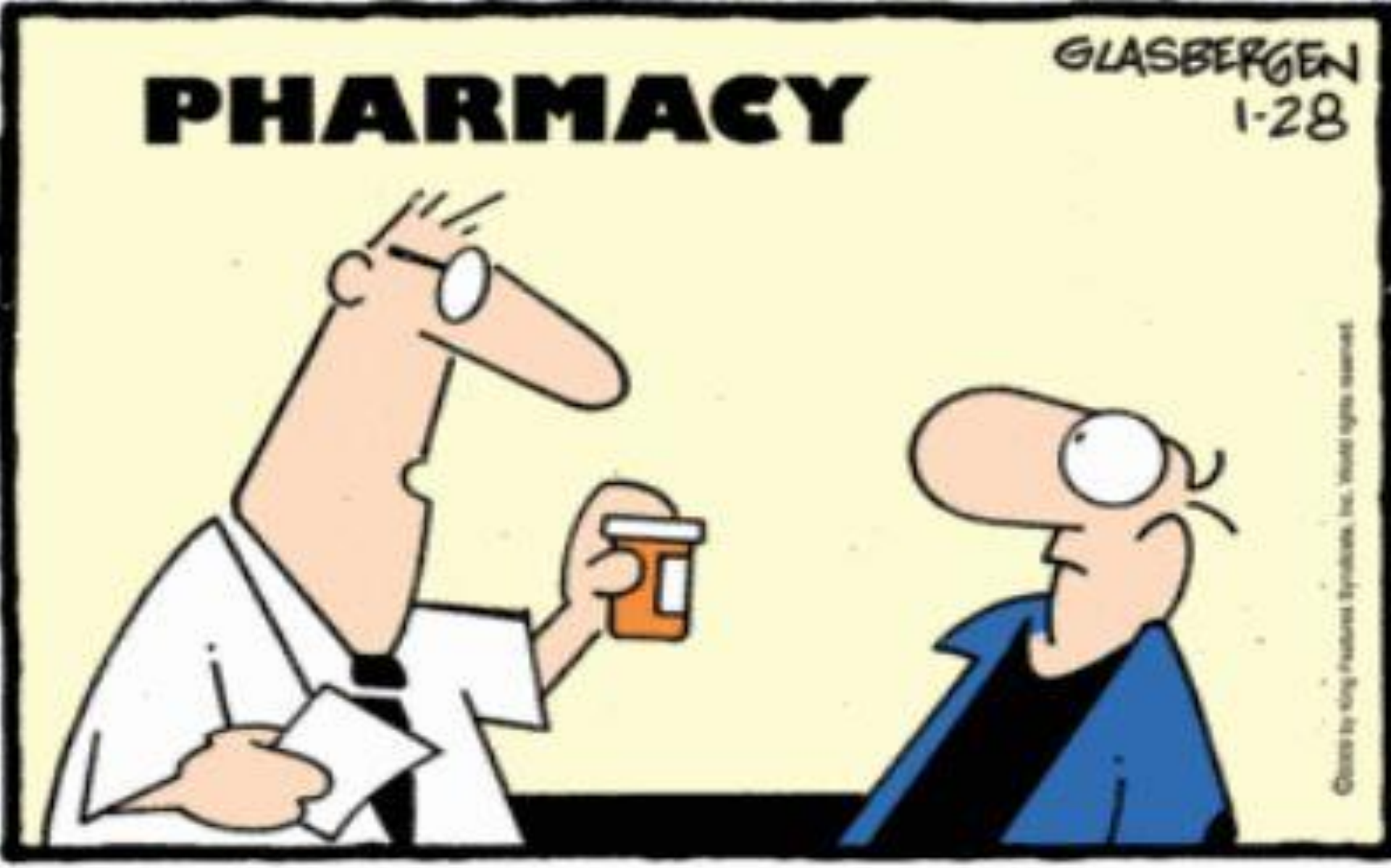
- How to measure and monitor the adherence to medications
- Hard to track the adherence to medications in daily practice

Clinical Trials

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- Poor Adherence / Compliance
  - Evaluating drug safety and efficacy
    - Primary outcome measures may show
      - Similarity between the placebo and non-adherent groups
      - Not detecting the side-effects due to non-adherence
      - Larger than expected differences between non-adherent participants and adherent participants

➔ Inaccurately magnify predictions of drug safety and efficacy



"It's an experimental drug. We're still testing to see how much customers will pay for it."

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Clinical Trials

- Adherence is closely monitored in clinical trials setting
- "Hawthorne effect" – Patients who are conscious of ongoing observation may demonstrate improved behaviour
- 20% reduction in drug adherence;

  ➔ > 50% increase in sample size
- What is adequate adherence?

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Medication Adherence in Clinical Trials

- Maximizing adherence;
  - Robust estimate of the test drug's efficacy leading to better informed strategic development decisions
  - Prevent increase in study costs from requiring larger samples to maintain power
  - Reduce unexplained variance in clinical drug development, ultimately shortening the development process

Methods of Measuring Adherence.

Table 1. Methods of Measuring Adherence.

Test	Advantages	Disadvantages
Indirect methods		
Patient questionnaires, patient self-reports	Simple; inexpensive; the most useful method in the clinical setting	Susceptible to error with increases in time between visits; results are easily distorted by the patient
Pill counts	Objective, quantifiable, and easy to perform	Data easily altered by the patient (e.g., pill dumping)
Rates of prescription refills	Objective; easy to obtain data	A prescription refill is not equivalent to ingestion of medication; requires a closed pharmacy system
Assessment of the patient's clinical response	Simple; generally easy to perform	Factors other than medication adherence can affect clinical response
Electronic medication monitors	Precise; results are easily quantified; tracks patterns of taking medication	Expensive; requires return visits and downloading data from medication vials
Measurement of physiologic markers (e.g., heart rate in patients taking beta-blockers)	Often easy to perform	Marker may be absent for other reasons (e.g., increased metabolism, poor absorption, lack of response)
Patient diaries	Help to correct for poor recall	Easily altered by the patient
When the patient is a child, questionnaire for caregiver or teacher	Simple; objective	Susceptible to distortion

Medication Adherence in Clinical Trials

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- What pharmacists can do to improve adherence?



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Methods

- Data from 30 participants enrolled in 8 different studies were chosen at random for review
- 15 participants from 4 studies – active counselling by pharmacists
- 15 participants from 4 studies – no counselling by pharmacists
- Oral medication for self-administration

Methods

- Measure of medication adherence – pill count

$$\% \text{ doses taken} = \frac{(\text{number of pills dispensed} - \text{number of pills left in bottle}) \times 100}{(\text{number of days between dispensed dates}) \times (\text{number of doses per day}) \times (\text{number of pills per dose})}$$

- Duration reviewed – 3 months to 36 months
- Dosing frequency – OD or BD matched between the two samples

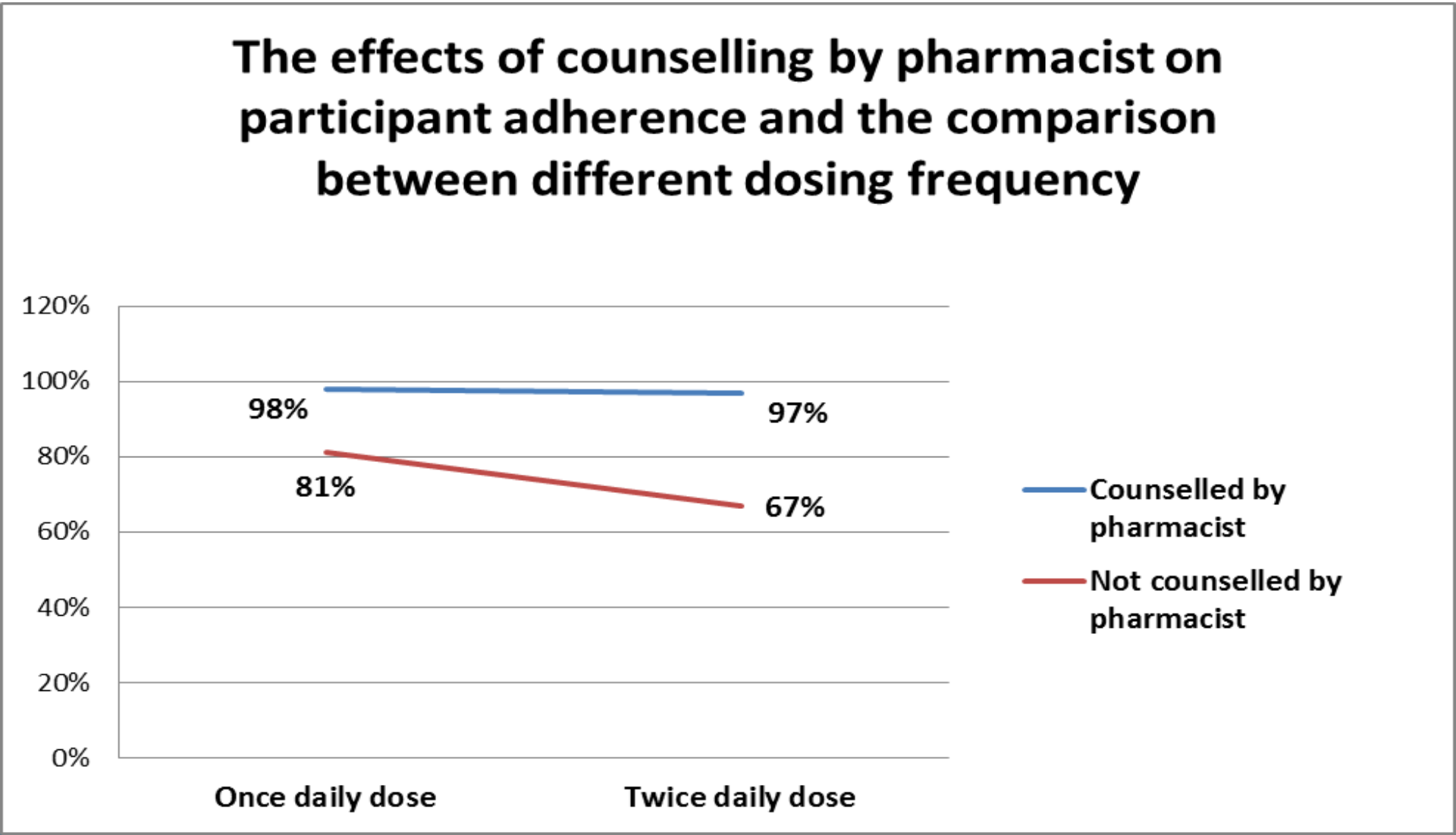
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Results

Dosing Frequency	Duration of medication adherence studied	% doses taken	
		Counselled by pharmacist	Not counselled by pharmacist
Once Daily	≤ 6 months	100%	88%
		99%	83%
		95%	88%
	> 6 months & ≤ 12 months	99%	83%
	> 12 months & ≤ 18 months	100%	74%
		99%	84%
	> 18 months	97%	91%
		98%	79%
Twice daily	≤ 6 months	97%	60%
		96%	50%
		100%	55%
	> 6 months & ≤ 12 months	95%	77%
	> 12 months & ≤ 18 months	93%	59%
		98%	94%
	> 18 months	99%	72%
Mean *(p<0.05)*		98%	76%

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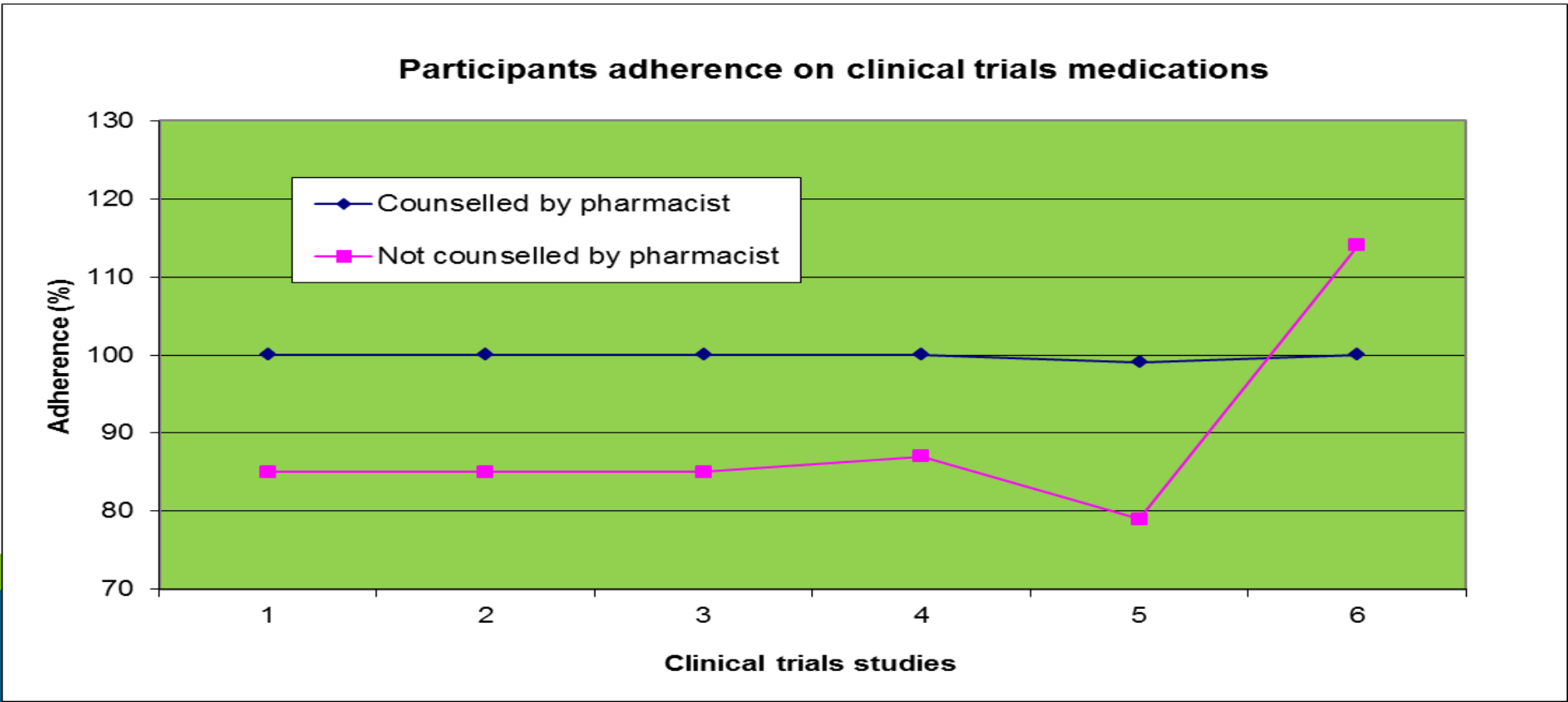
Results



Previous study in 2012

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- 99% adherence vs 89%
- Over-usage detected



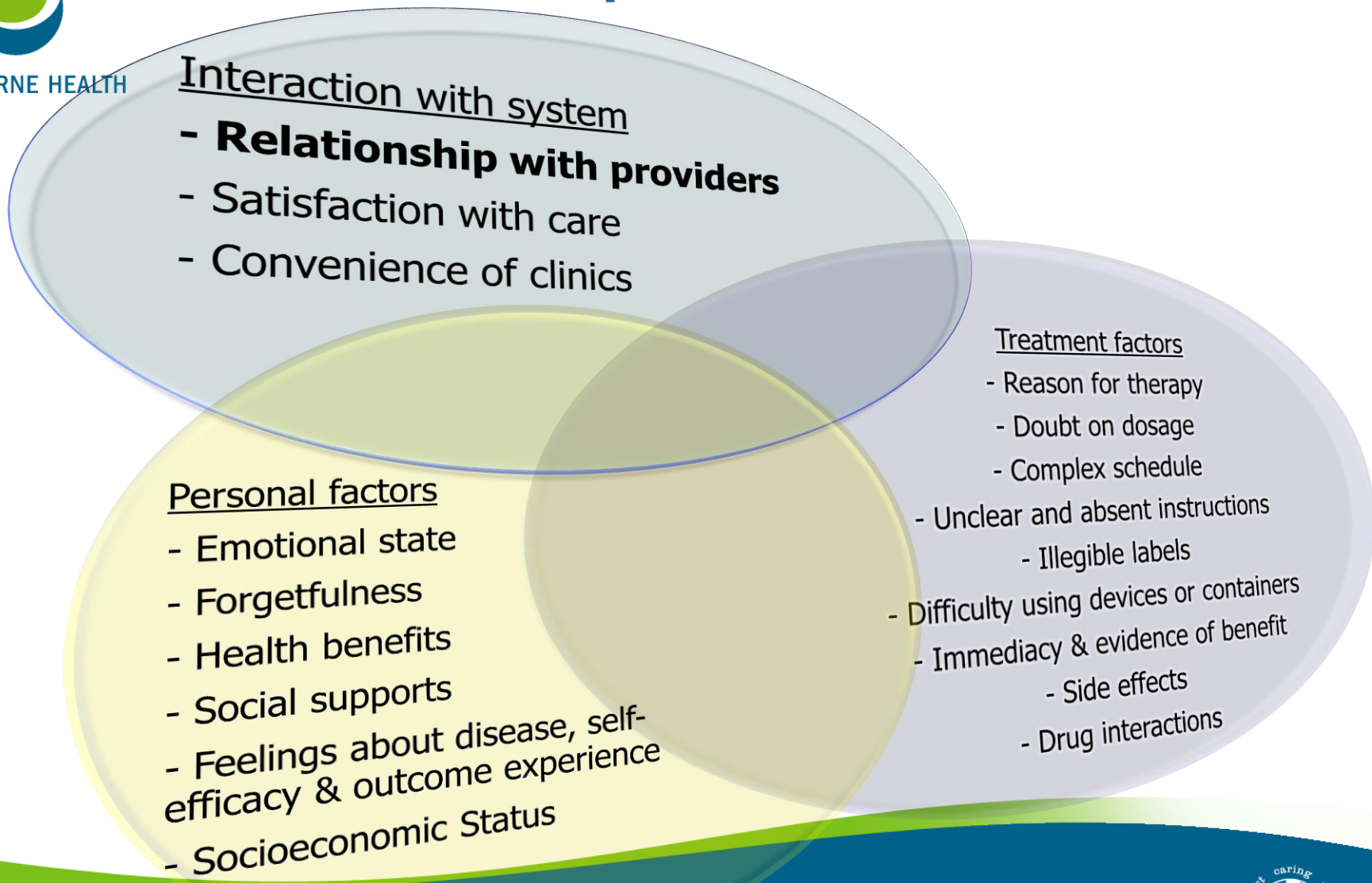
Pharmacist counselling on medication adherence

- Positive effect of pharmacist counselling on medication adherence in clinical trials setting
- Investigator's responsibility as per ICH GCP

4.6.6 The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product(s) to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.

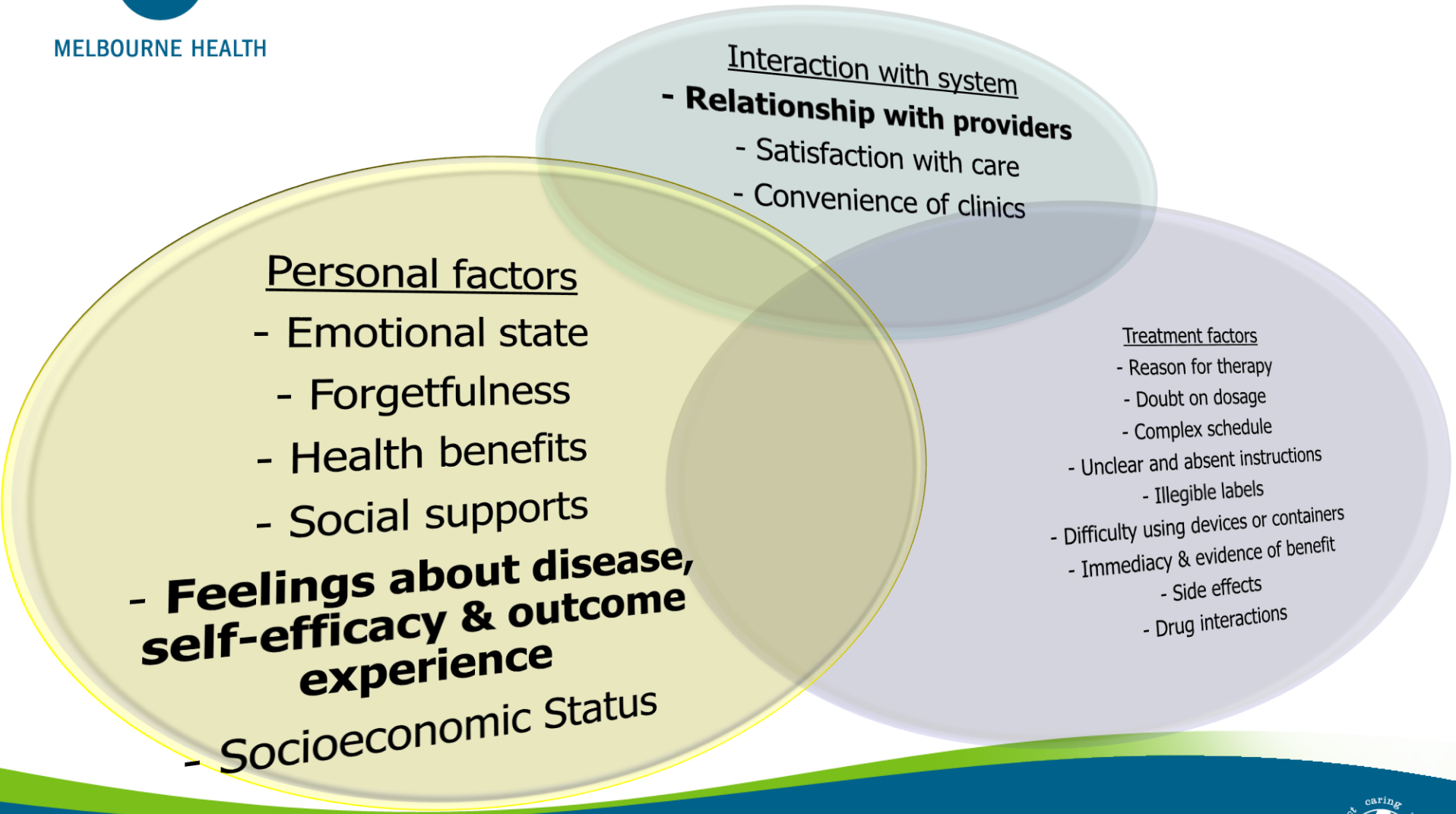
Reasons for poor adherence

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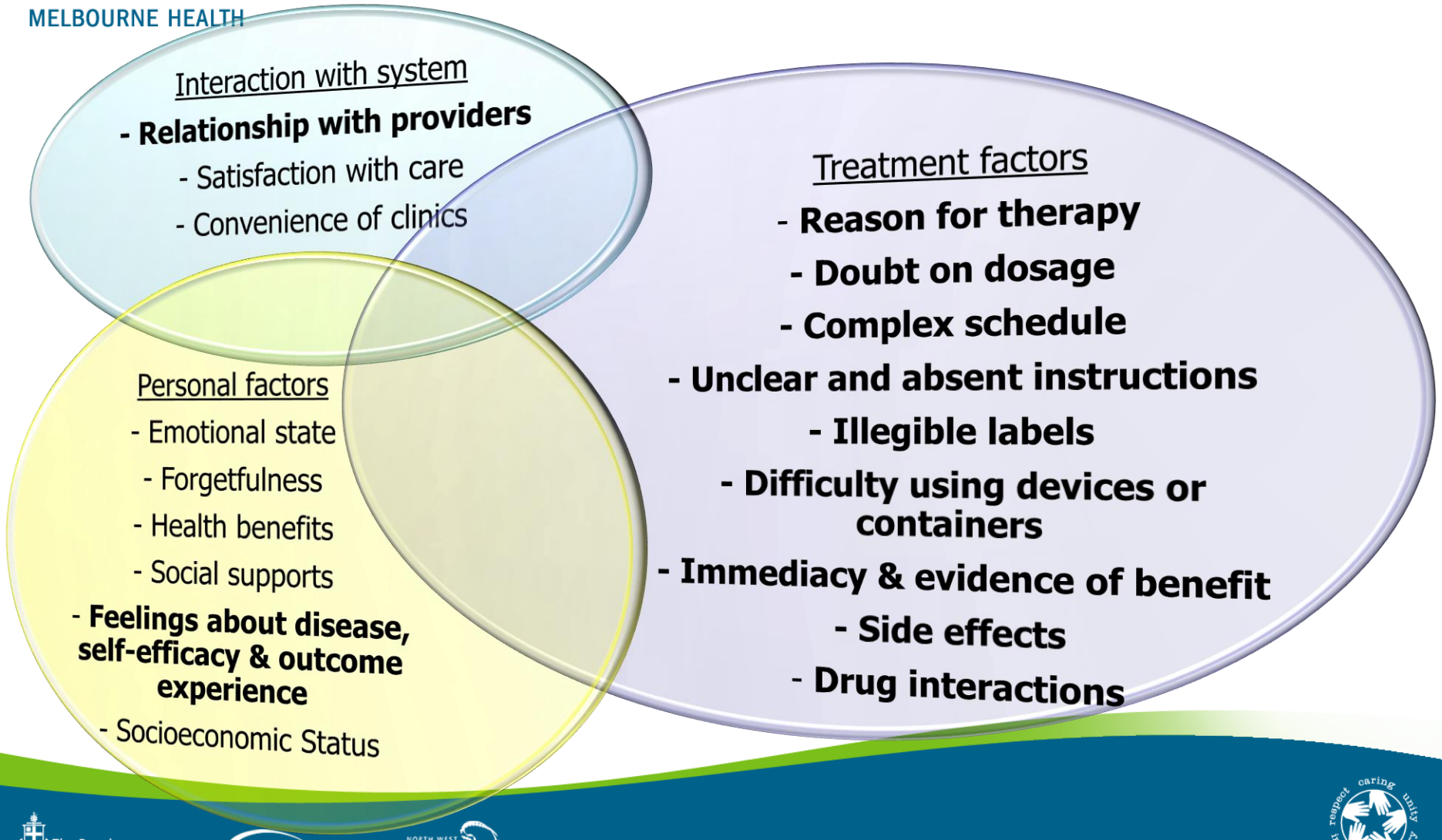
Reasons for poor adherence

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Reasons for poor adherence

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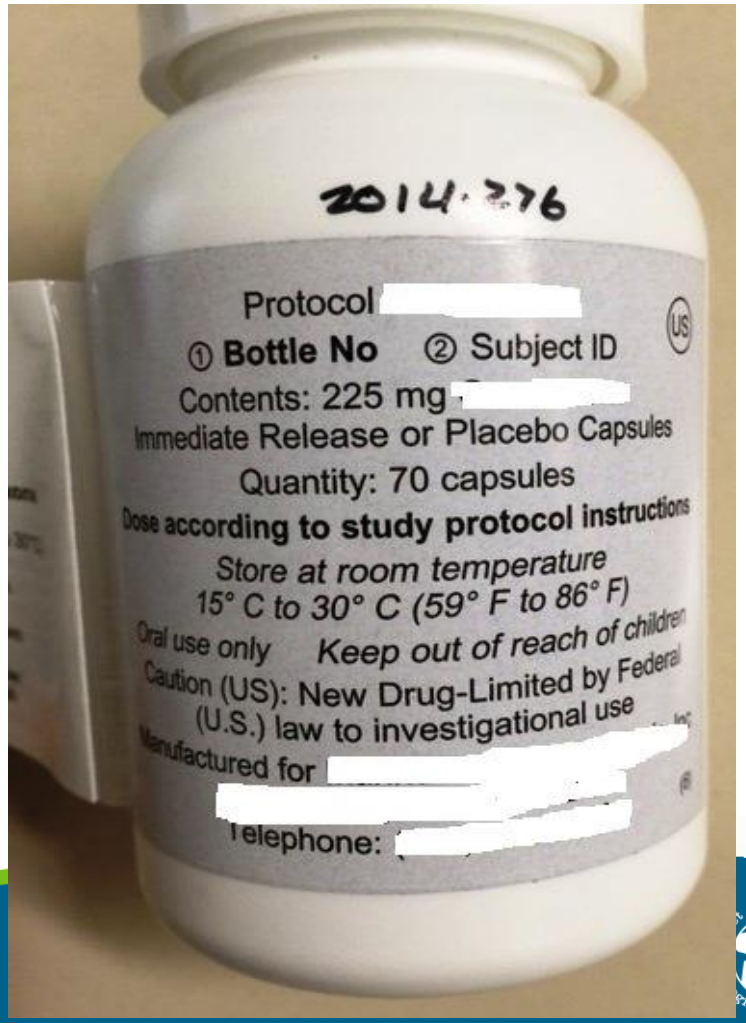
Administration of investigational medicines

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Table 1. Dosing Schedule for Cohort 1 Double Blind Phase, Open-Label Phase, and De-Escalation Period

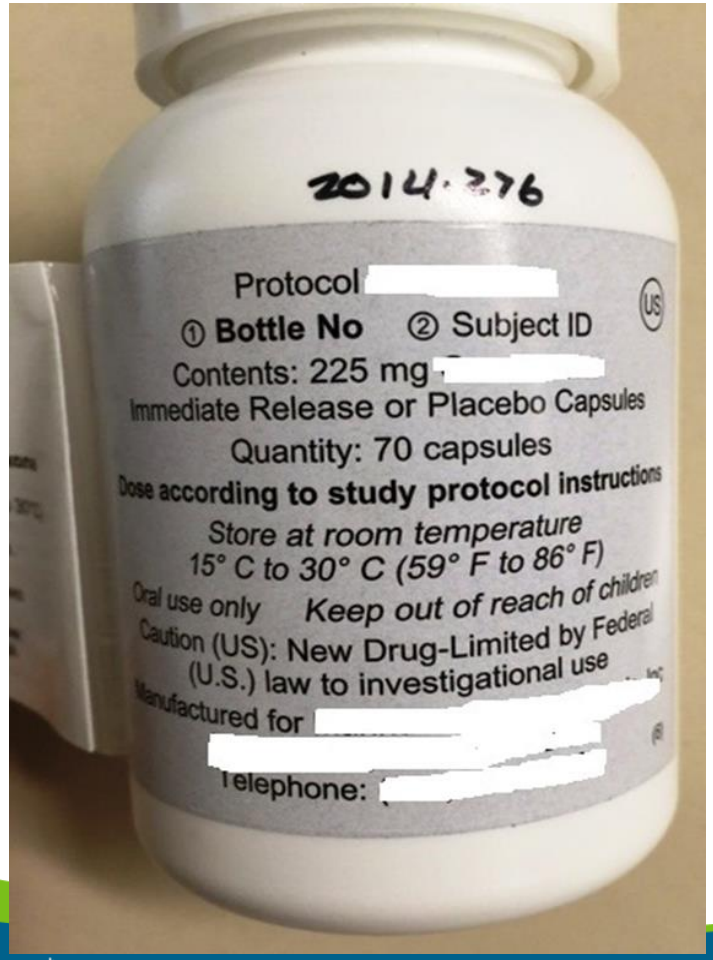
Cohort 1, Phase 1- Double Blind				
Visit	**Study Day**	**Dose (mg)/day**	**200 mg cap/day or matching placebo**	**225 mg cap/day or matching placebo**
Titration to 1200 mg/d (Visit 2)	1	400	2	0
	2	400	2	0
	3	800	4	0
	4	800	4	0
	5	1200	6	0
	6	1200	6	0
	7	1200	6	0
1200 mg/d Maintenance (Visit 3)	8- 35	1200	6	0
Step Titration to 1800 mg (Visit 4)	36	1800	0	8
1800 mg/d Maintenance	37-63	1800	0	8

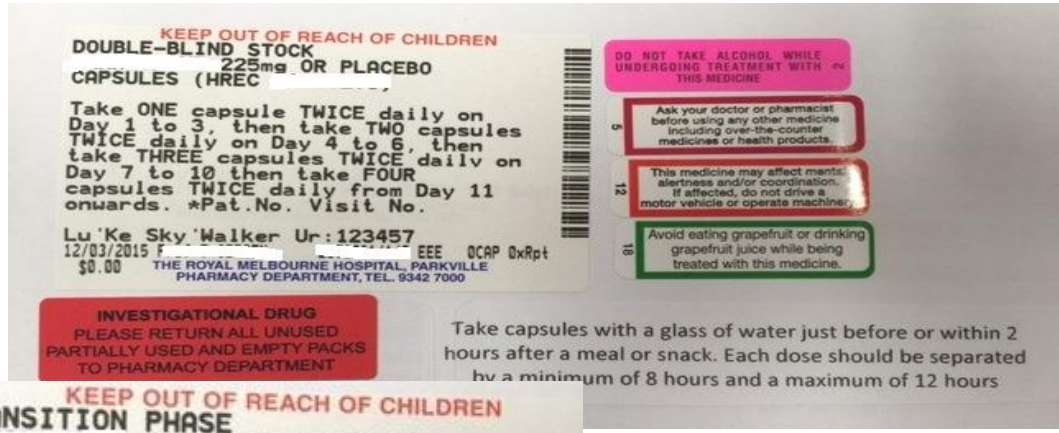
Cohort 1, Phase 2- Open Label					
DB Transition to Open-Label					
Visit	**Study Day**	**Dose (mg)/day**		**Bottle A 225 mg or PBO cap/day**	**Bottle B 225 mg or PBO cap/day**
				[redacted] 225 mg	[redacted] 225 mg
		[redacted]	**PBO/PBO**	**PBO: 225 mg**	**PBO: PBO**
Visit 5	64	1800	900	4	4
	65	1800	900	4	4
	66	1800	1350	6	2
	67	1800	1350	6	2
	68	1800	1350	6	2
	69	1800	1800	8	0
	70	1800	1800	8	0



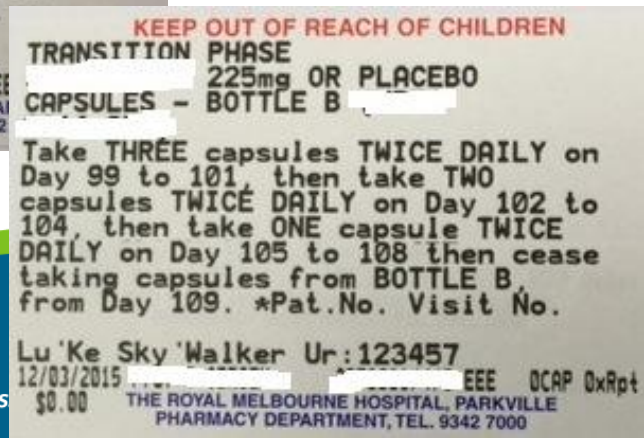
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Administration of investigational medicines

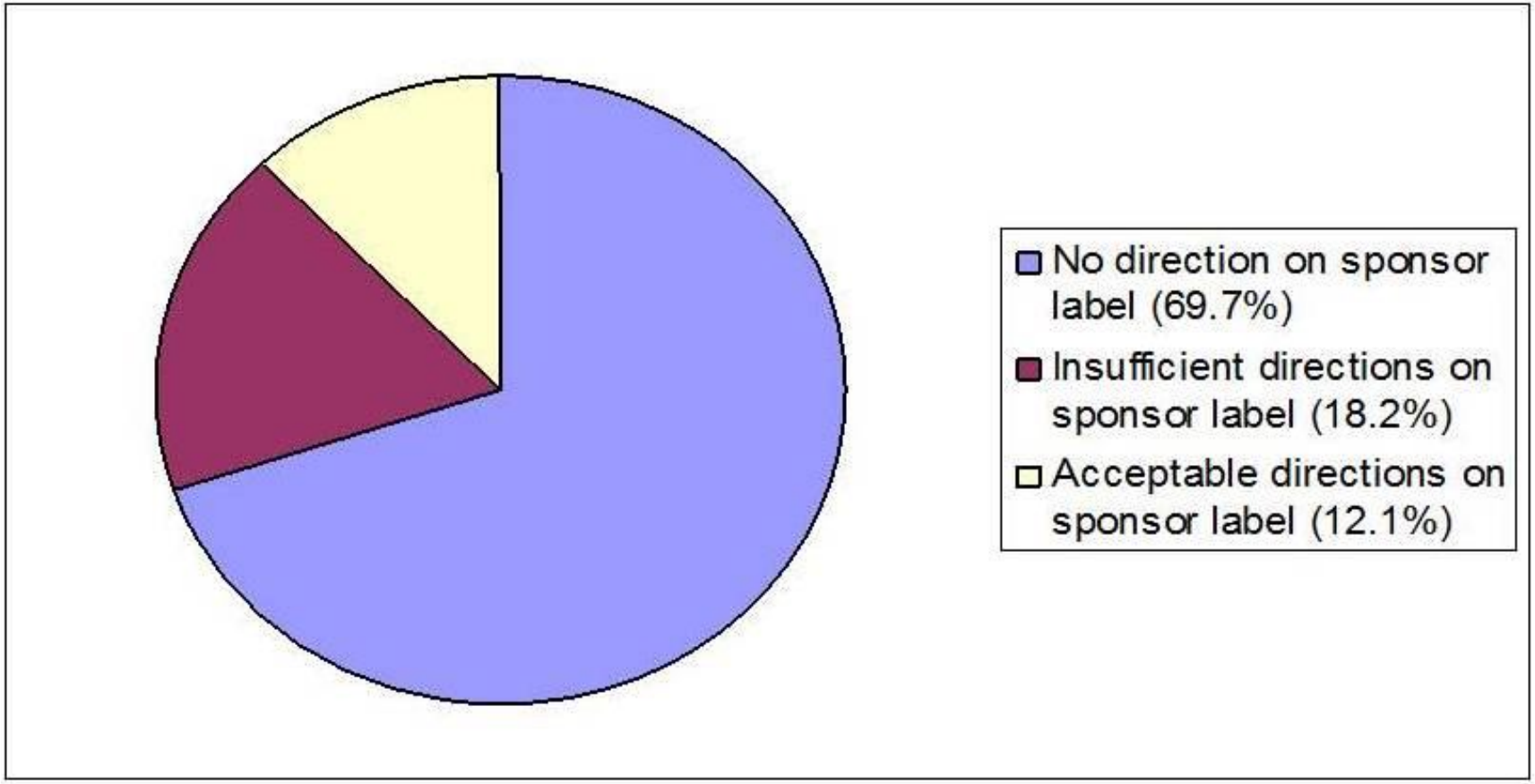








Sponsor labels on Investigational Medicines




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Clinical Trials Pharmacist

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- Has in-depth knowledge of pharmacotherapy and the study protocol
- Provides education to study participants;
  - Use and administration of investigational medicines
    - Correct doing instructions
    - Fasting requirements
    - Correct method of administration

Clinical Trials Pharmacist

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- Provides education to study participants;
  - Changes in formulation and dose strength
  - Prohibited and permitted concomitant medications
    - Over-the-counter medications
    - Alternative and complementary medications
    - Class action of any unlisted prohibited medications

Clinical Trials Pharmacist

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- Provides education to study participants;
  - Medicines information

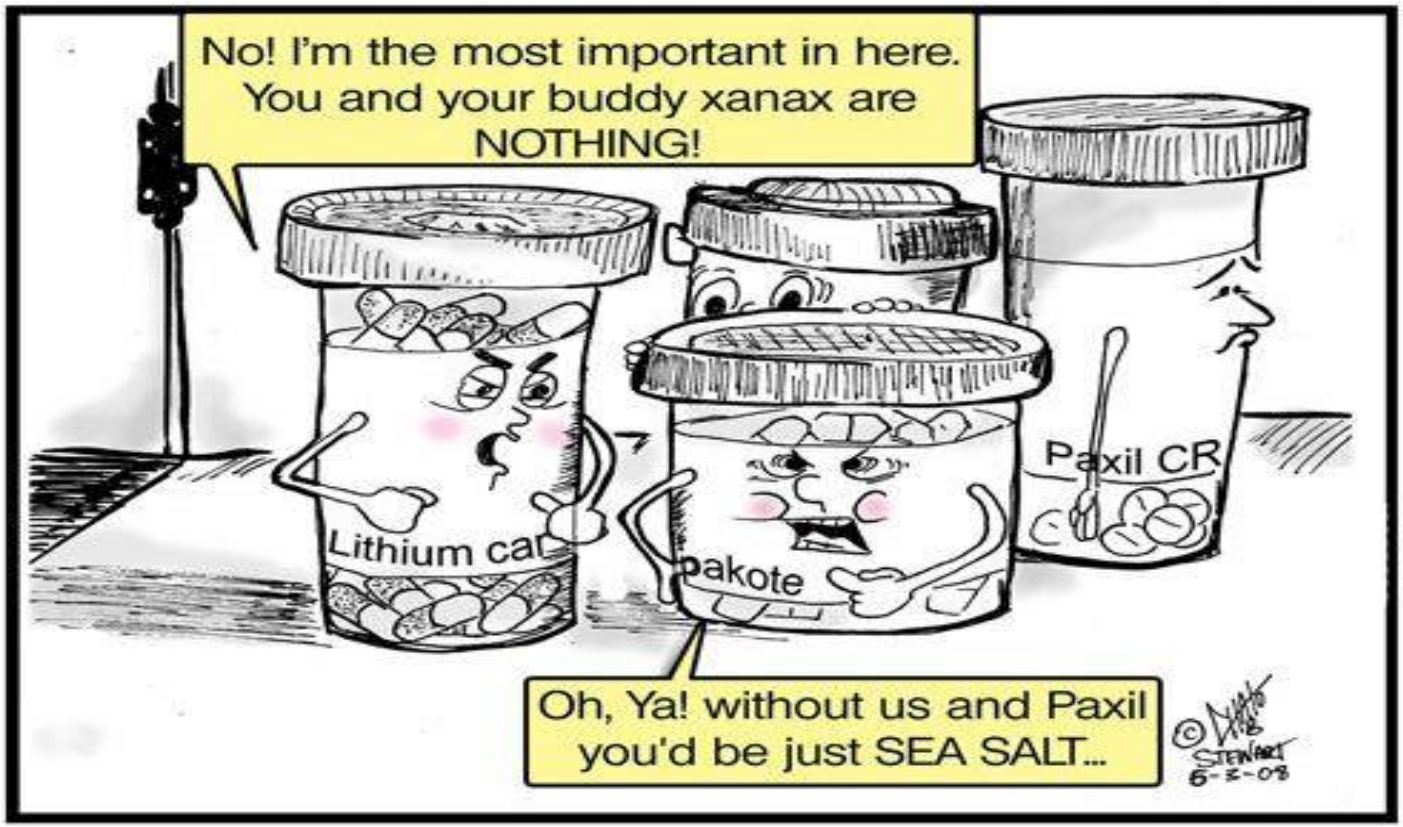


The Royal Melbourne Hospital

Clinical Trials Pharmacist

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- Provides education to study participants;
  - Drug interactions



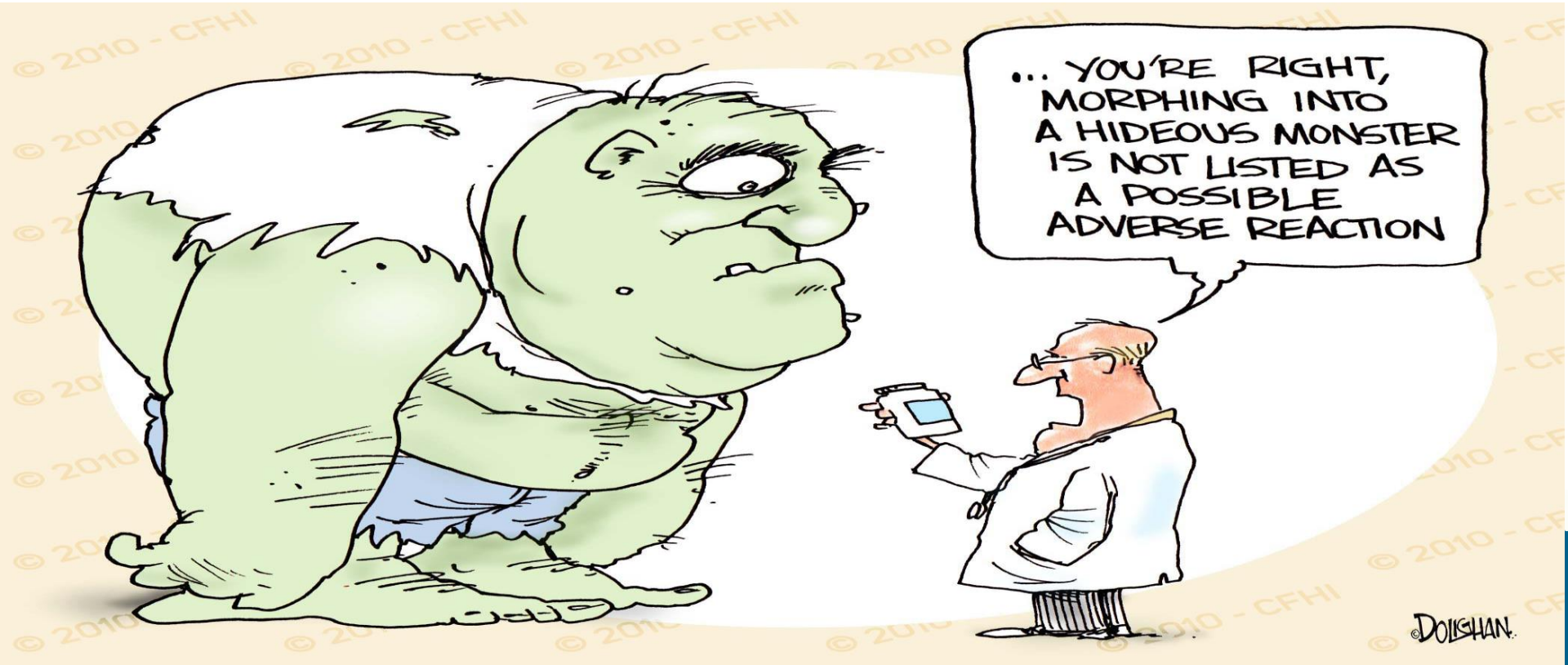
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NorthWestern Mental Health

Clinical Trials Pharmacist

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- Provides education to study participants;
  - Adverse drug reactions



British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2016) **82** 522–531 522

PHARMACOECONOMICS

What influences persistence with medicines? A multinational discrete choice experiment of 2549 patients

Correspondence Professor Dyfrig Hughes, Centre for Health Economics & Medicines Evaluation, Bangor University, Ardudwy, Normal Site, Bangor, Gwynedd, LL57 2PZ, UK. Tel.: +44 (0) 12 4838 2950; E-mail: d.a.hughes@bangor.ac.uk

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Emily A. F. Holmes[1], Valerie L. Morrison[2] and Dyfrig A. Hughes[1]

[1]*Centre for Health Economics & Medicines Evaluation, Bangor University, Bangor, UK and* [2]*School of Psychology, Bangor University, Bangor, UK*

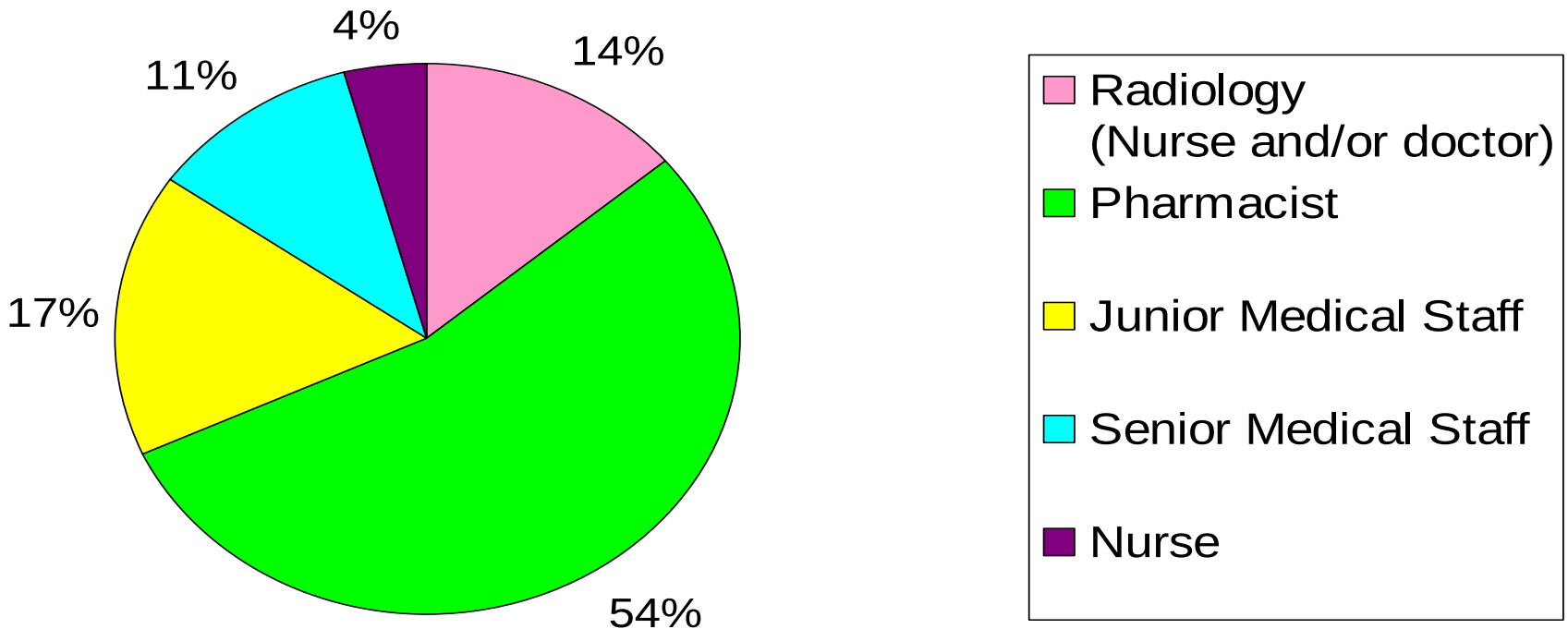
Keywords adherence, discrete choice experiment, medications, persistence, stated preference

The role of the clinical trials pharmacist in reporting of adverse drug reactions

The Royal Melbourne Hospital

Eugenia Hong, Emma Michael

Adverse Drug Reaction Reports 2011



submitted online, phone or by completing the "Blue Card".

participants.

Michael via email, eugenia.hong@mh.org.au or emma.michael@mh.org.au

Conclusion

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- The education and counselling of study participants by the clinical trials pharmacist could result in positive outcomes with regards to medication adherence
- This can be extended to outside the clinical trials setting


KEEP
CALM
I'M
A
PHARMACIST


KEEP
CALM
AND
ASK YOUR
PHARMACIST


KEEP
CALM
AND
DATE A
PHARMACIST


KEEP
CALM
AND
PARTY WITH A
PHARMACIST


KEEP
CALM
AND
HUG A
PHARMACIST


KEEP
CALM
and
TAKE YOUR
MEDS

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